UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/583,370	06/18/2007	Michel Dreano	SCHIAFFONATI 1	8192

1444 7590 09/12/2008

BROWDY AND NEIMARK, P.L.L.C.
624 NINTH STREET, NW
SUITE 300
WASHINGTON, DC 20001-5303

EXAMINER	
MERTZ, PREMA MARIA	
ART UNIT	PAPER NUMBER
1646	

MAIL DATE	DELIVERY MODE
09/12/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/583,370	DREANO ET AL.	
	Examiner	Art Unit	
	Prema M. Mertz	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 August 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *19,21-23,25,28,31-41,43-46,48,50,53-55 and 57-62* is/are pending in the application.

4a) Of the above claim(s) *33-39* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *19,21-23, 25, 28, 31-32, 40-41, 43-46, 48, 50, 53-55, 57-61* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 20, 24, 42, 47, and 49, have been canceled in the amendment filed 8/1/08 and claims 26-27, 29-30, 51-52, have been canceled previously. Amended claims 19, 21-23, 40-41, 43-45, 55, 57-58, previously presented claims 25, 28, 31-32, 46, 48, 50, 53-54, and new claims 59-62 (8/1/08) are pending in the instant application. Claims 33-39 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention.

2. Receipt of applicant's arguments and amendments filed on 8/1/2008 is acknowledged.

3. The following previous rejections and objections are withdrawn in light of applicants amendments filed on 8/1/2008:

(i) the rejection of claims 19-22, 28, 31-32, 40-42, 43, 45, 50, 53-54, 55-58, under 35 U.S.C. 102(b) as being anticipated by Kovalovich et al. (2001); and

(ii) the rejection of claims 19, 28, 31-32, 40-41, 43-48, 50, under 35 U.S.C. 102(b) as being anticipated by Selzner et al. (1999) .

4. Applicant's arguments filed on 8/1/08 have been fully considered and were persuasive in part. The issues remaining and new issues are stated below.

5. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Election/Restrictions

6. Applicant's argue that the specific dose range recited in independent claims 24 and 49 are now incorporated into independent claims 19, 40, 41 and 55, the present claims do indeed define a special technical contribution over Kovalovich and the prior art and therefore request

withdrawal of the restriction requirement. However, contrary to Applicants arguments, the methods of Groups 1-4 are patentably distinct from each other because each recites method steps not required by the other, each method uses different starting materials and patient populations and the search of all methods in one patent application would result in an undue search burden. Furthermore, a search for one method would not necessarily reveal art pertinent to any of the other methods and therefore, the search burden would be undue.

The Groups as delineated in the restriction requirement 1/28/2008 are patentably distinct one from the other such that each invention could, by itself, in principle, support its own separate patent (as shown by the arguments put forth in the written restriction requirement).

The requirement is still deemed proper and is therefore made FINAL.

Claims 33-39 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Claims 19, 21-23, 25, 28, 31-32, 40-41, 43-46, 48, 50, 53-55, 57-62, are drawn to the elected species and are under consideration by the Examiner.

Claim Rejections - 35 USC § 112, first paragraph, scope of enablement

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7a. Claims 19, 21-23, 25, 28, 31-32, 40-41, 43-46, 48, 50, 53-55, 57-62, are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of inducing proliferation of hepatocytes in CCl4 induced chemical cirrhosis, does not reasonably

provide enablement for a method for treating liver injury as recited in claim 1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

This rejection is maintained for reasons of record set forth at pages 3-8 of the previous Office action of 5/1/2008.

Applicants argue that Applicants have now amended the claims to be directed to "treating liver cirrhosis", as defined by DORLAND's ILLUSTRATED MEDICAL DICTIONARY, 30th edition, Saunders, 2000, "cirrhosis" is liver disease characterized by diffuse interlacing bands of fibrous tissue (i.e., scar tissue) dividing the hepatic parenchyma into micronodular or macronodular areas, and from the definition from Wikipedia that cirrhosis is simply scar tissue and nodules that are the result of injury or other liver tissue damage and it does not matter what causes the injury for one to get cirrhosis; cirrhosis is cirrhosis no matter what causes the damage. Applicants also argue that the present specification discloses at page 3, lines 8-12, that Kokudo et al., *J. Surg. Res.* 52:648-655 (1992) established that the carbon tetrachloride/phenobarbital model is a valid model for impaired liver regeneration and liver cirrhosis, where micronodular cirrhosis was achieved by simultaneous administration of carbon tetrachloride and Phenobarbital and Ortiz et al., J. Am.*Soc. Nephrol.* 7:2694-2699 (1996) reference and abstracts from three references, which are representative of the knowledge in the art that the carbon tetrachloride and phenobarbital model is recognized and understood to be a model for cirrhosis in general. Applicants also argue that Applicants did not discover the effect of IL-6 on liver injury; rather, this was reported by the Kovalovich in larger doses for various liver injuries based on the carbon tetrachloride/Phenobarbital model. However, Applicants arguments are non-persuasive

because even though the carbon tetrachloride/phenobarbital model is a model for impaired liver regeneration and liver cirrhosis, there are other factors that are responsible for cirrhosis. Cirrhosis can be caused by several disparate factors including alcohol (chemically induced cirrhosis) viruses (viral-induced cirrhosis) or hereditary factors. Pol et al (1998) disclose that alcohol and viral infection have different effects on the development of hepatitis and host-related and environmental cofactors play a role in the severity of cirrhosis (see abstract, page 12, column 2). Therefore, contrary to Applicants arguments, the presently amended claims are not commensurate with the scope of the specification.

Claim rejections-35 U.S.C. 112, second paragraph

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 19, 21-23, 25, 28, 31-32, 40-41, 43-46, 48, 50, 53-55, 57-62, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

This rejection is maintained for reasons of record set forth at pages 9-11 of the previous Office action of 5/1/2008.

Claim 19 remains rejected because the fails to recite "an effective amount" of IL-6. Applicants argue that the claims have been amended to recite the dose but claim 19 fails to recite "an effective amount" of the dose.

Claims 40, 41 and 55, remain vague and indefinite because they recite "an expression vector". A method of treatment by administering "an expression vector" has been restricted by the Examiner into a different Group and the restriction has been made final by the Examiner. It is suggested that this limitation be deleted form these claims to obviate this rejection.

Claims 21-23, 25, 28, 31-32, 42, 43-46, 48, 50, 53-54, 57-62 are rejected as vague and indefinite insofar as they depend on the above rejected claims for their limitations.

Claim rejections-35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in Graham v. John Deere Co., 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

9a. Claims 19, 21-23, 25, 28, 31-32, 40-41, 43-46, 48, 50, 53-55, 57-62, are rejected under 35 U.S.C. 102(b) as being unpatentable over Kovalovich et al. (2001)

Kovalovich et al discloses a method of treating liver injury caused by carbon tetrachloride treatment by administration of IL-6 at a dose of 1μg/g weight which protects against Fas-mediated death in the liver of mice by establishing a critical level of anti-apoptotic hepatic proteins FLIP, Bcl-2 and Bcl-xL (see abstract; see Figure 1, page 26606). However, the reference does not specifically teach administering to the mice a dose of at IL-6 in the range of 0.1 to 10 μg/kg weight.

It would have been *prima facie* obvious to one having ordinary skill in the art to vary the dosage of the IL-6 to be administered in the method disclosed by Kovalovich such that it includes administering the IL-6 at a dose in the range of 0.1 to 10 μg/kg weight to obtain the desired effect of administering IL-6.

One would have been motivated to vary the dosage to obtain the therapeutically effective amount to treat cirrhosis because it is well known in the art that cytokines are toxic at high doses and it would be desirable to obtain a therapeutically effective amount of IL-6 at the lowest dosage possible. Therefore it would have been obvious to the skilled artisan to vary the dosage and the results achieved would have been expected. Therefore, the Kovalovich reference renders obvious claims 19, 21-23, 25, 28, 31-32, 40-41, 43-46, 48, 50, 53-55, 57-62.

Conclusion

No claim is allowed.

Claims 19, 21-23, 25, 28, 31-32, 40-41, 43-46, 48, 50, 53-55, 57-62, are rejected.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Prema Mertz whose telephone number is (571) 272-0876. The examiner can normally be reached on Monday-Friday from 7:00AM to 3:30PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, can be reached on (571) 272-0835.

Official papers filed by fax should be directed to (571) 273-8300. Faxed draft or informal communications with the examiner should be directed to (571) 273-0876.

Information regarding the status of an application may be obtained from the Patent application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Prema Mertz/
Primary Examiner
Art Unit 1646